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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,310	11/21/2003	Paul G. Brunetta	P1979R1	3292

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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,310	BRUNETTA ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-17 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-17 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 8-17 and 32 are pending.

2. In view of the amendment filed 3/7/06, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 8-17 and 32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the antibody 2C4 produced by hybridoma cell line deposited under ATCC Deposit No HB-12697 recited in claims 3, 9, and 31 are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification.

It is noted that said hybridoma has been deposited with the ATCC as disclosed on page 44 of the specification under the Budapest Treaty.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the specific hybridoma under ATCC HB-12697 secreting said antibody 2C4 has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

Further, the specification does not teach how to treat psoriasis in all mammal comprising administering to the mammal a therapeutic effective amount of any antibody or antibody fragment Fab which binds any ErbB2, any antibody that blocks ligand

activation of any ErbB receptor, any monoclonal antibody that blocks binding of monoclonal antibody 2C4 to any ErbB2, any antibody that has which biological characteristic of monoclonal antibody 2C4, any antibody or antibody fragment Fab which binds any ErbB2 that is conjugated to a cytotoxic agent, any antibody that binds to any ErbB2 in combination with any secondary therapeutic agent or second drug such as any ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist for the claimed method.

The specification discloses only four monoclonal antibodies that bind specifically to human ErbB2 such as 7C2, 7F3, 4D5, and 2C4 produced by hybridomas under the ATCC accession number ATCC HB-12215, ATCC HB-12216, ATCC CRL 10463 and ATCC HB-12697, respective (page 44). The specification discloses humanized antibodies and binding fragment thereof (see pages 45, 8-11 and page 48). The specification further teaches the antibody such as 2C4 inhibits the association of ErbB2 and ErbB3 in mammary tumor cell lines MCF7 and SK-BR3 (see page 47). The specification further discloses that binding of monoclonal antibody 2C4 to human erbB2 blocks EGF, TGFα or HRG mediated activation of MAPK kinase in MCF7 cancer cells (see page 51). The specification asserts that that any non-malignant disease, any disorder including psoriasis *may be treated* with anti-ErbB2 antibody alone or co-administration of adjunct therapy (see page 53, lines 6-24, in particular). The specification at page 15 defines the term "treatment" referring to both therapeutic treatment and "prophylactic" or "preventive" measures. The specification does not teach any vitro assay that is predictive of preventing psoriasis in all mammals in vivo by administration of any antibody that binds to any ErbB2. There is no disclosure of psoriasis could be prevented by such antibody.

The specification does not teach any and all antibody that bind to human ErbB2 also bind to ErbB2 from other mammals. The specification is silent as to whether the deposited antibody 2C4 that binds to human ErbB2 also binds to erbB2 from other mammal, in turn, would be effective for treating psoriasis in all mammal. Given the unlimited number of antibody to any and all ErbB2, there is inadequate guidance as to the structure, such as, for example, CDR1-3 from the light chain and heavy chain of any and all antibody that bind to all ErbB2. The specification does not teach any assay to identify

which mammal within a given population who would or would not have psoriasis. The specification at page 15 defines the term "treatment" referring to both therapeutic treatment and "prophylactic" or "preventive" measures. The specification does not teach any vitro assay that is predictive of preventing psoriasis in all mammals in vivo by administration of any antibody that binds to any ErbB2. There is no disclosure of psoriasis could be prevented by such antibody.

With regard to antibody that blocks the binding of monoclonal antibody 2C4 to ErbB2, the specification does not disclose how blocking 2C4 from binding to ErbB2 is effective for treating/preventing psoriasis. The specification does not adequately describe such antibody.

With regard to claim 8, there is insufficient guidance as to which "biological characteristic" of monoclonal antibody 2C4 that any and all antibody should have for treating psoriasis and which "biological characteristic" of monoclonal antibody 2C4 that any and all antibody should have for preventing psoriasis. The term "comprises" in claim 9 is open-ended. There is insufficient guidance as to the binding specificity of any antibody that comprises antibody 2C4 or humanized 2C4.

With regard to claims 15 and 32, there is inadequate guidance as to any and all ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist without the chemical structure, much less which combination with antibody that binds to ErbB2 is effective for treating psoriasis and which combination is effective for preventing psoriasis.

With regard to cardioprotectant, the specification discloses at page 22 that cardioprotectant is a compound or composition which prevents or reduces myocardial dysfunction (i.e., cariomyopathy, and/or congestive heart failure) associated with administration of anti-ErbB2, there is no disclosure of any cardioprotectant in combination of anti-ErbB2 that could prevent myocardial dysfunction (i.e., cariomyopathy, and/or congestive heart failure associated with anti-ErbB2 treatment for psoriasis.

Given the unlimited number of antibody that binds to any ErbB2, there is not a single working example such antibody could treat psoriasis in human, much less for preventing psoriasis in all mammal.

Sauder et al, of record, teach psoriasis is a chronic T cell mediated inflammatory skin disease and no cure for psoriasis has ever been found (see page 206, col. 2, in particular). Sauder further teach the traditional options for psoriasis involves in the use of both topical and systemic medications such as topical corticosteroid, coal tar, salicylic acid, vitamin D derivative, phototherapy, methotrexate, or cyclosporine (see page 207-208, in particular).

Giaccone et al, of record, teach predicting the future for patients using EGF receptor targeted agent is unpredictable and further research is required before the optimal dosing strategy for HER1/EGFR tyrosine kinase inhibitor (see entire documents, abstract, in particular).

Further, there is insufficient guidance as how to make and use any "IL-1 antagonist", any "TNF antagonist", and any "ErbB antagonist" without the chemical structure or the amino acid sequence. It is known in the art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein.

Ngo et al, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Mason et al, of record, teach in activin A, even a single amino acid substitution from cysteine to alanine fails to maintain either the structure and/or functions such as intracellular assembly and secretion of the dimer protein (see page 327, column 1, in particular) and loss biological activity (See activin cysteine mutant 4 and 12, page 327, column 2, in particular) and loss of receptor binding activity (See Receptor Binding Activities of activin cysteine mutant 4 and 12, page 327, column 2, in particular). Mason *et al* further teach an equivalent protein such as TGFβ1 in which replacing cysteine residue for a serine residue, the resulting secreted monomer polypeptide lacks bioactivity (See page 330, column 1, first paragraph, in particular). Accordingly, undue amount of experimentation would be required to practice the claimed invention.

Given the unlimited number of non-malignant disorders, the lack of guidance as to structure of any antagonist as well as the binding specificity of any ErbB2 and the lack of in vivo working example, it would require undue experimentation of one skilled in the

art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Applicants' arguments filed 3/7/06 have been fully considered but are not found persuasive.

Applicants' position is that the specification as been amended to provide these specific assurances, which are further confirmed herein. Accordingly, this reason for rejection is moot. All claims currently pending relate to the treatment of psoriasis in a mammal, such as a human, by administration of a therapeutically effective amount of an antibody that binds ErbB2. The only question is whether the treatment of psoriasis with an ErbB2 antibody is enabled. The claims are not directed to a cure of psoriasis. Antibodies that bind ErbB2 were well known in the art at the priority date of the present application. There is no requirement in patent law to support the claims by working examples. Nonetheless, the specification contains a specific example (Example 4) teaching the use of ErbB2 antibodies such as rhuMab 2C4 or humanized 7F3 to treat psoriasis.

In response to the argument with respect to the deposit issue, simply amending the specification is insufficient to overcome this rejection because an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the specific hybridoma under ATCC HB-12697 secreting said antibody 2C4 has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

In contrast to applicants' assertion that specification contains a specific example (Example 4) teaching the use of ErbB2 antibodies such as rhuMab 2C4 or humanized 7F3 to treat psoriasis, the use of MCF7 breast cancer cell is not an appropriate model for a method of treating psoriasis. This is because psoriasis is a chronic T cell mediated inflammatory skin disease and no cure for psoriasis has ever been found (see page 206, col. 2, in particular). Psoriasis involved in the proliferation-differentiation of ErbB2 expression in keratinocytes. The art does not teach the use of breast cancer cell as a model for psoriasis. The specification does not teach any and all antibodies that bind to

human ErbB2 also bind to ErbB2 from other mammals. The specification is silent as to whether the deposited antibody 2C4 that binds to *human* ErbB2 also binds to erbB2 from other mammal, in turn, would be effective for treating/ preventing psoriasis in other mammal. Given the unlimited number of antibody to any and all ErbB2, there is inadequate guidance as to the structure, such as, for example, CDR1-3 from the light chain and heavy chain of any and all antibody that bind to all ErbB2. The specification does not teach any assay to identify which mammal within a given population who would or would not have psoriasis. The specification at page 15 defines the term "treatment" referring to both therapeutic treatment and "prophylactic" or "preventive" measures. The specification does not teach any vitro assay that is predictive of preventing psoriasis in all mammals in vivo by administration of any antibody that binds to any ErbB2. There is no disclosure of psoriasis could be prevented by such antibody.

With regard to antibody that block the binding of monoclonal antibody 2C4 to ErbB2, there is no disclosure of any antibody that blocks monoclonal antibody 2C4 from binding to ErbB2 is effective for treating and preventing psoriasis. The specification does not adequately describe such antibody. The specification does not disclose binding antibody 2C4 to ErbB2 causes psoriasis and that antibody blocking said 2C4 antibody from binding to any ErbB2 is effective for treating psoriasis, let alone preventing psoriasis.

With regard to claim 8, there is insufficient guidance as to which "biological characteristic" of monoclonal antibody 2C4 that any and all antibody should have for treating psoriasis and which "biological characteristic" of monoclonal antibody 2C4 that any and all antibody should have for preventing psoriasis. The term "comprises" in claim 9 is open-ended. There is insufficient guidance as to the binding specificity of any antibody that comprises antibody 2C4 or humanized antibody 2C4.

With regard to claims 15 and 32, there is inadequate guidance as to any and all ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist without the chemical structure, much less which combination with antibody that binds to ErbB2 is effective for treating or preventing psoriasis.

With regard to cardioprotectant, the specification discloses at page 22 that cardioprotectant is a compound or composition which prevents or reduces myocardial dysfunction (i.e., cariomyopathy, and/or congestive heart failure) associated with administration of anti-ErbB2, there is no disclosure of any cardioprotectant in combination of anti-ErbB2 that could prevent myocardial dysfunction (i.e., cariomyopathy, and/or congestive heart failure associated with anti-ErbB2 treatment for psoriasis. Accordingly, undue experimentation would be required to practice the claimed method in which any antibody binds to any ErbB2 in all mammals.

5. Claims 1-3, 8-17 and 32 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) any and all antibody that bind to any ErbB2 for treating psoriasis in all mammal, (2) any antibody that blocks binding of monoclonal antibody 2C4 to ErbB2 for a method of treating psoriasis in all mammal, (3) any antibody that has which "biological characteristic" of monoclonal antibody 2C4 for a method of treating psoriasis in all mammal, (4) any antibody that has which biological characteristic of monoclonal antibody 2C4 wherein the antibody "comprises" monoclonal antibody 2C4 or humanized 2C4 for the claimed method, and (5) any second therapeutic agent or second drug such as any ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist for the claimed method.

The specification discloses four monoclonal antibodies that bind specifically to human ErbB2 such as 7C2, 7F3, 4D5, and 2C4 produced by hybridomas under the ATCC accession number ATCC HB-12215, ATCC HB-12216, ATCC CRL 10463 and ATCC HB-12697, respective (page 44). The specification discloses humanized antibodies and binding fragment thereof (see pages 45, 8-11 and page 48). The specification further teaches the antibody such as 2C4 inhibits the association of ErbB2 and ErbB3 in mammary tumor cell lines MCF7 and SK-BR3 (see page 47). The specification further discloses that binding of monoclonal antibody 2C4 to human erbB2 blocks EGF, TGFα

or HRG mediated activation of MAPK kinase in MCF7 cancer cells (see page 51). The specification asserts that that any non-malignant disease, any disorder including psoriasis *may be treated* with anti-ErbB2 antibody alone or co-administration of adjunct therapy (see page 53, lines 6-24, in particular). The specification at page 15 defines the term "treatment" referring to both therapeutic treatment and "prophylactic" or "preventive" measures. The specification does not teach any vitro assay that is predictive of preventing psoriasis in all mammals in vivo by administration of any antibody that binds to any ErbB2. There is no disclosure of psoriasis could be prevented by such antibody.

The specification does not adequate describe any and all antibody that bind to ErbB2 from other mammals. The specification is silent as to whether the deposited antibody 2C4 that binds to human ErbB2 also binds to erbB2 from other mammal, in turn, would be effective for treating psoriasis in all mammal. Given the unlimited number of antibody to any and all ErbB2, there is inadequate written description about the structure, i.e., CDR1-3 from the light chain and heavy chain of all antibody that bind to all ErbB2 for the claimed method. There is inadequate written description about any and all antibody that block the binding of monoclonal antibody 2C4 to ErbB2, in turn, the undisclosed antibody is effective as a method of treating psoriasis in all mammal. It is not clear how blocking 2C4 from binding to ErbB2 is effective for the claimed method. The specification does not adequately describe such antibody.

With regard to claim 8, there is inadequate written description about which "biological characteristic" of monoclonal antibody 2C4 that any and all antibody should have for treating psoriasis. The term "comprises" in claim 9 is open-ended. There is inadequate written description about any antibody that comprises antibody 2C4 or humanized 2C4.

With regard to claims 15 and 32, there is inadequate written description about of any and all ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist without the chemical structure, much less in combination with antibody that binds to ErbB2 for treating psoriasis. Further, it is not clear how cardioprotectant is being use for treating psoriasis where the disease is associated with epidermal keratinocytes in the skin.

With the exception of the specific deposited antibodies that bind to human ErbB2 in combination with the specific IL-1 antagonist or TNF antagonist for inhibiting the association of ErbB2 and ErbB3 in mammary tumor cell lines, i.e., MCF7 and SK-BR3 in vitro, there is insufficient written description about the other antibody and ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist as broadly as claimed for the method.

The specification discloses four specific deposited antibodies that bind to human ErbB2 as disclosed at page 44, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of antibody that bind to any and all ErbB2, and second therapeutic agent or second drug for treating or preventing psoriasis in all mammals. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 3/7/06 have been fully considered but are not found persuasive.

Applicants' position is that in support of the rejection, as it applies to the amended claims, the Examiner states that the specification does not reasonably provide a written description of the binding specificity of all antibodies that bind any ErbB2. This statement is incorrect and is refuted by the Examiner's own acknowledgement that the specification discloses a series of antibodies binding ErbB2 along with their binding fragments. Such antibodies are not only described in the present application but have been deposited and are available from the ATTC, and their sequences have been described in published documents (incorporated by reference), well before the priority date of the present application. From the statement that there is "inadequate written description about the binding specificity of all antibody" (Page 7 of the Office Action), it appears that the Examiner believes that the disclosure of the binding specificity of every single antibody within the genus of antibodies binding ErbB2 would be required to meet to written description requirement for the genus. This is clearly not the proper legal

standard. Since the "non-malignant disease" is now specified as "psoriasis", Applicants do not claim a genus of non-malignant disease and the species of psoriasis is adequately described throughout the specification, such as, for example, at page 17, lines 4-8; page 39, line 33-page 43, line 38 and in Example 5. Furthermore, immunosuppressive agents are sufficiently described throughout the specification, such as, for example, at page 21, lines 12-32 of the specification.

In response, the amended claim 1 still recites a method of treating psoriasis in all mammal in which the method comprises administering any and all antibody which binds ErbB2. The specification does not adequate describe any and all antibodies that bind to ErbB2 from other mammals for the claimed method. The specification is silent as to whether the deposited antibody 2C4 that binds to *human* ErbB2 also binds to erbB2 from other mammal, in turn, would be effective for treating psoriasis in all mammals, much less for preventing psoriasis. Given the unlimited number of antibody to any and all ErbB2, there is inadequate written description about the structure, i.e., CDR1-3 from the light chain and heavy chain of all antibody that bind to all ErbB2 for the claimed method.

With regard to claim 3, there is inadequate written description about any antibody that blocks the binding of monoclonal antibody 2C4 to human ErbB2 and whether such undisclosed antibody is effective as a method of treating/preventing psoriasis in all mammals. The specification does not adequately describe such antibody. Further, it is not clear how blocking 2C4 from binding to ErbB2 is effective for the claimed method. This is because 2C4 antibody binding to ErbB2 is not the cause for psoriasis. The specification does not disclose monoclonal 2C4 is an autoantibody that binds to ErbB2 in vivo and any antibody that blocks 2C4 antibody binding to ErbB2 is effective for treating psoriasis.

With regard to claim 8, there is inadequate written description about which "biological characteristic" of monoclonal antibody 2C4 that any and all antibodies should have for treating psoriasis. The term "comprises" in claim 9 is open-ended. There is inadequate written description about any antibody that comprises antibody 2C4 or humanized 2C4.

With regard to claims 15 and 32, there is inadequate written description about of any and all ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any

cardioprotectant any cytokine, and any TNF antagonist without the chemical structure, much less in combination with antibody that binds to ErbB2 for treating psoriasis. Further, it is not clear how cardioprotectant is being use for treating psoriasis where the disease is associated with epidermal keratinocytes in the skin.

With the exception of the specific deposited antibodies that bind to human ErbB2 in combination with the specific IL-1 antagonist or TNF antagonist for inhibiting the association of ErbB2 and ErbB3 in mammary tumor cell lines MCF7 and SK-BR3 in vitro, there is insufficient written description about the other antibody and ErbB antagonist, any immunosuppressive agent, any chemotherapeutic agent, any cytotoxic agent, any growth inhibitory agent, any EGFR-targeted drug, any tyrosine kinase inhibitor, any anti-angiogenic agent, and anti-hormonal compound, any cardioprotectant any cytokine, and any TNF antagonist as broadly as claimed for the method.

The specification discloses four specific deposited antibodies that bind to human ErbB2 as disclosed at page 44, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of antibody that bind to any and all ErbB2, and second therapeutic agent or second drug for treating psoriasis. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

6. The following new ground of rejection is necessitated by the amendment filed 3/7/06.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-2, 8-17, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/15730 publication (of record, March 8, 2001; PTO 1449) in view of WO 98/02540 (of record, January 22, 1998; PTO 1449) and Feldman et al (of record, Dermatol Online J 6(1): 4, September 2000; PTO 892).

The WO 01/15730 publication teaches a method of treating a benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular) by administering to a mammal such as human, dogs, horses, (see abstract, page 14, lines 4-8, in particular) an effective amount of an antibody which binds ErbB2 such as humanized version of 4D5 also known as HERCEPTIN®, 7C2, 7F3, 4D5, 2C4 (see page 33, in particular). The reference monoclonal antibody 2C4 obviously blocks the ErbB2 ligand from activating its receptor, ErbB2. The reference antibody 2C4 obviously has a biological characteristic of monoclonal antibody 2C4. The WO 01/15730 publication further teaches the humanized form of 2C4 (see page 5, lines 34, in particular) and antibody fragment thereof such as Fab or Fv (see page 11, lines 26-37, page 12-13, in particular). The reference antibody is not conjugated to with a cytotoxic agent (see page 33, page 14, lines 30-33, claim 1 of WO 01/15730 publication, in particular). The WO 01/15730 publication teaches administering to the patient such as human a second therapeutic agent such as chemotherapeutic agent (see page 14, lines 34-38 through page 15, lines 1-29, in particular), a growth inhibitory agent (see page 15, lines 30 through page 16, lines 1-2, in particular), or anti-ErbB2 or binding fragment thereof conjugated to a cytotoxic agent such as bacterial toxin (see page 25, lines 31-39, page 26, lines 1-11, in particular). The reference antibody is administered at least one dose to the patient in an about from 4mg/kg not exceeding 30mg/kg, which is within the claimed limitation of about 0.5mg/kg to about 30 mg/kg.

The claimed invention differs from the teachings of the reference only in that the method wherein the disease is psoriasis.

The WO 98/02540 publication teaches ErbB2 plays a role in psoriasis and a method of treating psoriasis by administering to the mammal with an agent that blocks

the ErbB2 ligand from binding to its receptor ErbB2 such as soluble ErbB2 receptor that comprises extracellular domain of ErbB2 fused to IgG (see page 35, line 11, homodimer, abstract, in particular). The WO 98/02540 publication teaches blocking ErbB2 using ErbB antagonist such as ErbB2 and ErbB3 or ErbB2 and ErbB4 fused to Fc prevents the ErbB ligand from binding and activation of the ErbB receptor (see page 25, lines 1-10, page 23, lines 23-31, heterodimer, abstract, claims 37-40, in particular).

Feldman et al teach a method of treating psoriasis that involved inflammation, hyperproliferation of keratinocyte by administering to the patient various immunosuppressive agent or a combination of such agents such as corticosteroid (steroid), cyclosporine, retinoid, psoralens, coal tar, and phototherapy such as UVB, methotrexate (see entire document, abstract, summary, in particular). Feldman et al teach a combination of modalities can be utilized to enhance the therapeutic effect and minimize the adverse effects that could result from excessive use of one agent (see Treatment goal, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat psoriasis by substituting the ErbB2-IgG that blocks ErbB2 ligand from binding to ErbB2 as taught by the WO 98/02540 publication for the antibody or Fab that binds to ErbB2 and thereby preventing the binding of ErbB2 ligand to its receptor as taught by the WO 01/15730 publication in combination with a second therapeutic agent such as immunosuppressive agent, chemotherapeutic agent or cytotoxic agent as taught by the WO 01/15730 publication or immunosuppressive agent or anti-inflammatory agent such as corticosteroid (steroid), cyclosporine, retinoid, psoralens, coal tar, and phototherapy such as UVB, methotrexate that are useful for treating psoriasis as taught by Feldman et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because blocking ErbB2 ligand from binding to ErbB2 receptor is useful for treating psoriasis as taught by the WO 98/02540 publication (see page 35, line 11, homodimer, abstract, in particular). The WO 01/15730 publication teaches antibody that binds specifically to ErbB2 is useful for treating hyperproliferative epithelial, inflammatory and angiogenic immunological disorders (see page 14, lines 9-14, page 30, lines 31-38, in particular). Feldman et al teach a method of treating psoriasis that involved in inflammation and

hyperproliferation of keratinocyte by administering to the patient various immunosuppressive agent or a combination of such agents such as corticosteroid, cyclosporine, retinoid, psoralens, coal tar, and phototherapy such as UVB, methotrexate (see entire document, abstract, summary, in particular). Feldman et al teach a combination of modalities can be utilized to enhance the therapeutic effect and minimize the adverse effects that could result from excessive use of one agent (see Treatment goal, in particular).

Applicants' arguments filed 3/7/06 have been fully considered but are not found persuasive.

Applicants' position is that claims 1, 15, 16 and 32 have been amended. Claims 4-7, 18-19, and 29-31 have been canceled. The WO 01/15730 publication does not teach a method of treating psoriasis. The use of ErbB2 antibodies to treat psoriasis is not explicitly disclosed in WO 01/15730 publication. Even if WO 01/15730 publication and WO 98/157030 could be properly combined, they would still not make obvious the claimed invention.

In response to applicants' argument that WO 01/15730 publication does not teach the use of ErbB2 antibodies to treat psoriasis, this rejection would have been rejected under 35 U.S.C. 102(b) had the WO 01/15730 publication teach the use of ErbB2 antibodies to treat psoriasis. The teachings of the WO 01/15730 publication pertaining to the use of ErbB2 antibodies to treat benign hyperproliferative epithelial, inflammatory angiogenic immunological disorders, the teachings of the WO 98/02540 publication pertaining to a method of treating psoriasis by blocking the ErbB2 ligand from binding to its receptor ErbB2 using soluble ErbB2 receptor that comprises extracellular domain of ErbB2 fused to IgG while the teachings of Feldman et al pertaining to treating psoriasis that involved in inflammation and hyperproliferation of keratinocyte by administering to the patient various immunosuppressive agent, anti-proliferative and anti-inflammatory agent would have lead to one of ordinary skill in the art with the expectation of success in treating psoriasis by substituting the soluble ErbB2 that blocks ErbB2 ligand from binding to its receptor as taught by the WO 98/02540 publication for the antibody that binds to ErbB2 and preventing the ErbB2 ligand from binding to its receptor as taught by WO 01/15730 publication in combination with various immunosuppressive agent, inflammatory and anti-proliferative agent that are known for treating psoriasis as taught by Feldman et al.

10. Claim 3 is free of prior art.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

14. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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